

Endometritis caused by *Chlamydia trachomatis*

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SUMMARY *Chlamydia trachomatis* was found to be the aetiological agent of endometritis in three women with concomitant signs of salpingitis. All patients developed a significant antibody response to the organism. Chlamydia were recovered from aspirated uterine contents of two patients and darkfield examination of histological sections showed chlamydial inclusions in endometrial cells in one patient. Thus, *C trachomatis* can be recovered from the endometrium of patients in whom the cervical culture result is negative. In one patient curettage showed endometritis with a characteristic plasma-cell infiltration. The occurrence of chlamydial endometritis may explain why irregular bleeding is a common finding in patients with salpingitis. It also suggests a canalicular spread of chlamydia from the cervix to the Fallopian tubes.

Introduction

Chlamydia trachomatis has been associated with cervicitis¹ and salpingitis,² and perihepatitis may occur in women with chlamydial genital infection.³

Salpingitis caused by chlamydia⁴ and gonococci⁵ are histologically similar. Gonococcal salpingitis is an endosalpingitis and the infection spreads to the Fallopian tubes from the cervix via the endometrium.⁵ Experimental salpingitis in monkeys has indicated that *C trachomatis*, like *Neisseria gonorrhoeae*, also spreads canalicularly to the Fallopian tubes.⁶

In this study, we present evidence that endometritis is another manifestation of genital chlamydial infection.

Methods

SAMPLING TECHNIQUE

Urethral, cervical, and rectal specimens

Specimens for culture were collected by rotating swabs in the cervical canal and the urethra after the cervical os and the urethral orifice had been exposed using a sterile speculum inserted into the vagina. Specimens for *C trachomatis* were collected by cotton-tipped aluminium swabs and for *Mycoplasma*

hominis and *Ureaplasma urealyticum* by cotton-tipped wooden sticks. Specimens for the isolation of *N gonorrhoeae* from the cervix and rectum were collected with cotton-tipped wooden swabs treated with charcoal.

Endometrial contents

For the collection of endometrial contents, a plastic tube (armoured with a mandrin) was introduced through the cervical canal. After the mandrin had been replaced by a baby-feeding tube adapted to a syringe, the contents of the uterine cavity were aspirated.

Fallopian tubes

Minute biopsy specimens from the fimbriae of the Fallopian tubes were collected at laparoscopy from two of the patients. After the specimens had been crushed in physiological saline, cotton-tipped swabs were soaked with the mixture for culturing.

Serological tests

Serum and cervical secretion were collected for serological tests. The cervical secretion was absorbed by a sponge and later eluted with phosphate-buffered saline.

The techniques of performing laparoscopy⁷ and the protected vacuum aspiration of the uterine contents⁸ have been described elsewhere.

MICROBIOLOGICAL METHODS

The cultural and serological methods used were those described.³

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Patients

CASE 1

In August 1978 an 18-year-old nulliparous woman underwent a legal abortion in the twelfth week of pregnancy. She attended again about two weeks after the operation, after having had lower abdominal pain and vaginal discharge for some days. Pelvic examination showed tenderness over both adnexae and a palpable mass in the left adnexal region. Her rectal temperature was 37.7°C , and the erythrocyte sedimentation rate (ESR) was 52 mm/first hour.

Acute salpingitis was diagnosed and she was treated with penicillin 2 megaunits and streptomycin 1 g by mouth daily for five days. She was discharged after seven days, when her symptoms had subsided and her temperature and ESR were normal.

She was readmitted five months later, after having lower right abdominal pain and nausea for some days. Physical examination indicated peritonitis. Pelvic examination could not be performed properly because of tenderness. Her temperature was 38.3°C and the ESR 22 mm/first hour.

Because of peritonitis of unknown aetiology, she underwent laparotomy, which showed a right-sided ovarian cyst ($10 \times 9 \times 8$ cm in size) and a right-sided pyosalpinx. The left Fallopian tube was fibrous and surrounded by adhesions, indicating earlier tubal infection. The appendix appeared normal. The right ovary and pyosalpinx were removed. Histological examination showed a pyosalpinx and an ovarian teratoma together with a mucous cystadenoma.

Postoperatively, she was treated with penicillin 2 megaunits, streptomycin 1 g, and metronidazole 600 mg by mouth daily for five days. The postoperative course was uneventful, and the patient was sent home 10 days after the operation.

Six months later she attended because of sterility. Pelvic examination showed an indolent cystic mass in the left adnexal region. Hysterosalpingography showed that the remaining tube was occluded and the uterine cavity was irregular in shape.

Because of irregular menstrual bleeding in February 1980 a curettage was performed at mid-cycle. Histological examination showed plasma-cell endometritis and dysplasia (figure). There were also signs of inflammation of the cervical mucosa. The

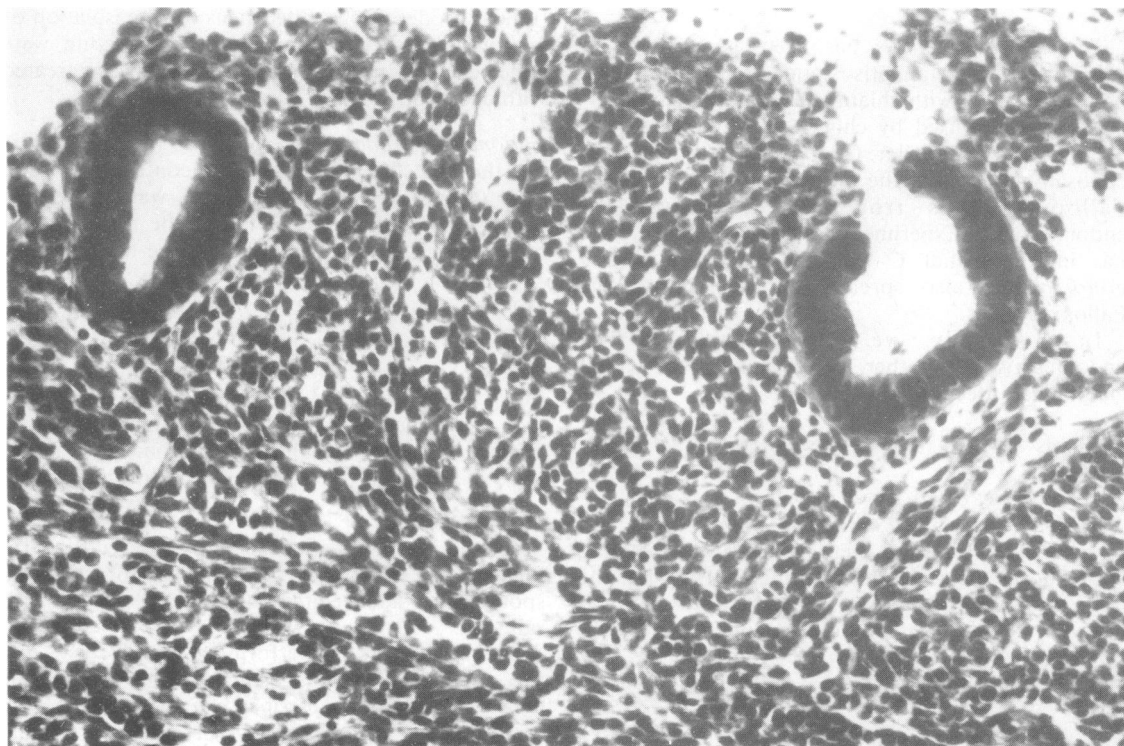


FIGURE Section of uterine endometrium of case 1. Marked inflammation with diffuse infiltration by a large number of plasma cells and some lymphocytes. Stained with haematoxylin and eosin ($\times 400$).

TABLE Results of chlamydial antibody tests

| Case No | Days after onset of abdominal pain | MIF chlamydial antibody titre | | | | |
|---------|------------------------------------|-------------------------------|------|--------------------|-----|-----|
| | | Serum | | Cervical secretion | | |
| | | IgM | IgG | IgM | IgG | IgA |
| 1 | 2 | 16 | 32 | ND | ND | ND |
| | 9 | 0 | 128 | — | — | — |
| | 800 (approx) | <8 | 64 | — | — | — |
| 2 | 4 | ND | ND | ND | ND | ND |
| | 26 | <8 | 512 | — | — | — |
| | 36 | <8 | 4096 | — | 64 | 8 |
| | 61 | <8 | 2048 | — | 128 | 8 |
| 3 | 6 | <8 | 16 | — | 32 | — |
| | 16 | <8 | 256 | — | 128 | — |
| | 42 | <8 | 256 | — | 16 | — |

ND = not done; — = antibodies not demonstrated; MIF = microimmunofluorescence

patient was then treated with erythromycin 1 g by mouth daily for 14 days.

In August 1978 cervical cultures had grown *C trachomatis* and *U urealyticum*. In February 1979 *C trachomatis* was again recovered from the cervix but no treatment was given. On this occasion *C trachomatis* was also isolated from the endometrium, and the mucosa of the extirpated right Fallopian tube showed numerous intracytoplasmic chlamydial inclusions. *N gonorrhoeae* was never isolated. The titres of microimmunofluorescence antibodies to *C trachomatis* changed significantly during the stay in hospital in 1978 (table). No antibodies to *M hominis*, *N gonorrhoeae*, or *U urealyticum* were detected.

CASE 2

A 19-year-old previously healthy nulliparous woman attended on 17 April 1980 after one month's history of irregular bleeding and pain in the lower abdomen. Three weeks before admission she had attended because of similar symptoms. On that occasion, a cervical culture grew *C trachomatis*, but no treatment was given.

At the second admission, pelvic examination showed tender adnexal masses and a yellowish discharge. Microscopical examination of a wet smear of vaginal contents showed moderate leucorrhoea. Her rectal temperature was 37.5°C. The ESR was 90 mm/first hour, and the white blood cell (WBC) count was $10.3 \times 10^9/l$ ($10\ 300/mm^3$).

Laparoscopy showed reddened swollen Fallopian tubes surrounded by fresh adhesions. The appendix was red and adherent to the right tube. Because of this finding, appendicectomy was performed. Histological examination of the appendix showed peri-appendicitis with normal mucosa.

Cultures for *C trachomatis*, *M hominis*, *N gonorrhoeae*, and *U urealyticum* from cervical swabs all gave negative results on two samples collected on

different occasions. Cultures from the endometrial aspirate and from a minute specimen of the fimbriae of the right Fallopian tube grew *C trachomatis*. *U urealyticum* was isolated from the endometrial aspirate but not from any other specimen.

The microimmunofluorescence tests showed a significant change in the titre of serum IgG chlamydial antibodies. Antibodies to *C trachomatis* in cervical secretion were not detected on the day of admission, but 10 days later both IgG and IgA chlamydial antibodies were found (table). No antibodies to *M hominis* or *N gonorrhoeae* were detected.

The patient was taking part in an antibiotic double-blind study, for which the code has not yet been broken. Ten days after admission her symptoms had subsided and she was discharged. A follow-up examination one month later showed no abnormalities.

CASE 3

A 36-year-old parous (2) woman attended on 11 February 1980 after five days of lower abdominal and back pain accompanied by bleeding. She had an intrauterine contraceptive device (IUCD) in situ since 1972. Pelvic examination showed bleeding and a tender mass in the left adnexal region. The IUCD was removed on the day of admission and laparoscopy showed red swollen Fallopian tubes with pus in the abdominal orifice of both. On admission her rectal temperature was 37.5°C, the ESR 46 mm/first hour, and the WBC count $10.8 \times 10^9/l$ ($10\ 800/mm^3$).

Cervical cultures grew *C trachomatis*, *M hominis*, and *U urealyticum*, while cultures from a minute specimen of the fimbriae of the right Fallopian tube were sterile. *C trachomatis* was also isolated from endometrial cultures. A significant change in the titre of IgG chlamydial antibodies in both serum and cervical secretion was found (table). No serum

antibodies to *M hominis* or *N gonorrhoeae* were detected.

The patient was taking part in the same antibiotic study as case 2. Her symptoms had subsided 10 days after admission, when she was discharged. One month later, a pelvic examination showed no abnormality.

Discussion

This study indicates that chlamydia may ascend from the cervix and infect the uterine mucosa and suggests that chlamydia can spread canalicularly via the endometrium to the Fallopian tubes.

Difficulties are encountered in the diagnosis of endometritis. It has been disputed whether chronic or subchronic endometritis between puberty and the menopause exists as a clinical and pathological entity. In this study, the diagnosis of acute endometritis was based, in two cases, on clinical and microbiological findings, whereas in case 1, the patient with chronic endometritis, histological examination was also performed.

An acute onset of irregular vaginal bleeding in non-pregnant patients with signs of cervicitis or salpingitis or both can indicate acute endometrial infection. Such bleeding occurred in cases 2 and 3. Bleeding or a bloody discharge may also occur in patients with so-called chronic endometritis (as in case 1), probably as a result of impaired endometrial responsiveness to ovarian hormones.⁹

In patients with acute non-tuberculous salpingitis bleeding into the uterine cavity from the tubes, or via the tubes from the abdominal cavity, was not observed during laparoscopy of more than 2000 patients with salpingitis treated in Lund, Sweden, during the 1970s (unpublished observations). This suggests that the endometrium is the site of the bleeding frequently seen in patients with salpingitis.

Some workers require histological examination of the endometrium after curettage to establish the diagnosis of endometritis. However, others consider this to be of limited value because of the difficulty of detecting the patchily localised inflammatory changes occurring in endometritis caused by sexually transmitted diseases such as gonorrhoea.⁵

The physiological leucocytic infiltration occurring in the endometrium during the late secretory phase of the menstrual cycle may be dense⁹ and follicular collections of lymphocytes are frequently seen in the endometrium of premenopausal women.¹⁰ Infiltration of the endometrium with a small, or even moderate, number of plasma cells can be the result of normal menstrual changes. However, the finding of more than a few plasma cells in the endometrium in

the follicular or ovulatory phases probably indicates the presence of chronic endometritis. A dense plasma-cell infiltration with round cells and polymorphonuclear leucocytes, as in case 1, probably warrants this diagnosis. An associated tubal inflammatory lesion is also generally seen in such cases, including case 1.¹¹

Runge⁵ cites reports on the clinical picture and histological and microbiological findings in patients with gonococcal endometritis. A gonococcal infection can spread from the cervical mucosa to the endometrium, thereby causing irregular intermenstrual bleeding and pain. Histologically there are usually patchy changes, initially with a large number of polymorphonuclear leucocytes, which are later replaced by lymphocytes and plasma cells. Gonococcal infection may be confined to the uterus and disappear spontaneously after the endometrium is shed in the following menstrual bleeding, but it can remain in the endometrial mucosa left after menstruation and cause chronic endometritis. Gonococcal endometritis may also spread canalicularly from the uterus to the Fallopian tubes.⁵

Cultural and serological tests did not indicate that the patients in this study had been earlier, or were currently, infected with *N gonorrhoeae*; they were culture-negative and none had gonococcal pillar antibodies.¹²

Chlamydial⁴ infection of the Fallopian tubes induces histopathological changes,⁴ which are very similar to those caused by *N gonorrhoeae*.⁵ This similarity is also apparent in experimental chlamydial infections in grivet monkeys.⁶ Gonococci and chlamydia¹³ both induce uterine mucosal histological changes that are very similar.

This study indicates that chlamydia can provoke acute endometritis with fever and intermenstrual bleeding. Little is yet known of the contribution of the uterus itself to the symptomatology of acute salpingitis. The present study suggests that chlamydial endometritis can explain the menorrhagic bleeding, which is a common finding in salpingitis, in which *C trachomatis* is one of the most important aetiological agents.²

Chlamydial infection of the uterine mucosa may even persist for years, as suggested by the history of case 1. Chronic chlamydial infection of the uterine tubes has recently been reported in women undergoing laparoscopy because of infertility.¹⁴ Although the endometrium is regularly shed in menstruating women, a chlamydial infection of the uterus might persist, because the organisms probably also infect the epithelium of the endometrial crypts. However, it cannot be ruled out that this patient (case 1) might have become reinfected shortly before taking part in the study.

It is noteworthy that in chlamydial infections of the upper female genital tract, involving the epithelium of the uterus and the Fallopian tubes, cervical cultures may give negative results, as in case 2. The method used for sampling from the uterus was designed to avoid contamination from the cervix. The failure to recover mycoplasmas and ureaplasmas from the endometrial aspirates of chlamydia-positive cases suggests the design of the sampling method is suitable for its purpose.

In addition to *C. trachomatis*, ureaplasmas were isolated from the specimen aspirated from the uterus of one of the patients. *U. urealyticum* has been recovered from the Fallopian tubes and cul-de-sac of patients with signs of acute salpingitis.¹⁵ However, *U. urealyticum*¹⁶ did not provoke salpingitis and parametritis in grivet monkeys in contrast to *C. trachomatis*¹² and *M. hominis*,¹⁷ which did.

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